

CLAIMS

A method of analysis which comprises:
a) providing a nucleotide target including a nucleotide at a specified position, an oligonucleotide probe, tethered to a support, said probe being complementary to the target and terminating at or near the specified position; and performing the steps:
i) incubating the target with the probe to form a duplex;
ii) incubating the duplex under ligation conditions with a nucleotide complementary to the target, and monitoring ligation in b) as an indication of the presence of the specified position in the target.

A method of analysis which comprises:
a) providing a nucleotide target having a variable number repeat section, and an oligonucleotide probe having a sequence complementary to the repeat section and a flanking sequence; and performing the steps:
i) incubating the target with the probe to form a duplex;
ii) incubating the duplex with a labelled nucleotide under chain extension conditions; and monitoring chain extension as an indication of the presence of the variable number repeat section of the target.

A method as claimed in claim 2, where the probe is tethered to a support.

A method as claimed in claim 2 or 3, where a DNA polymerase and/or ligase is used in step b).

1. A method of analysis which comprises: providing a polynucleotide target including a nucleotide at a specified position, and an oligonucleotide probe, tethered to a support, said probe being complementary to the target and terminating at or close to the said specified position; and performing the steps:
- a) incubating the target with the probe to form a duplex,
- b) incubating the duplex under ligation conditions with a labelled oligonucleotide complementary to the target,
- c) and monitoring ligation in b) as an indication of a point mutation at the specified position in the target.
2. A method of analysis which comprises: providing a polynucleotide target having a variable number tandem repeat section and a flanking section, and an oligonucleotide probe having a section complementary to the repeat section and a flanking section of the target; and performing the steps:
- a) incubating the target with the probe to form a duplex,
- b) incubating the duplex with a labelled oligonucleotide and/or at least one labelled nucleotide under chain extension conditions,
- c) and monitoring chain extension as an indication of the length of the variable number repeat section of the target.
3. A method as claimed in claim 2, wherein the probe is tethered to a support.
4. A method as claimed in claim 2 or claim 3, wherein a polymerase and/or ligase is used in step b).

5. A method as claimed in any one of claims 2 to 4, wherein the polynucleotide target has a variable number tandem repeat section and two flanking sections, and wherein in step b) a labelled oligonucleotide is ligated to the probe strand of the duplex.
- 5 6. A method as claimed in any one of claims 2 to 4, wherein the polynucleotide target has a variable number tandem repeat section and two flanking sections, and wherein in step b) the probe strand of the duplex is chain extended by addition of labelled nucleotides.
7. A method as claimed in any one of claims 1 to 6, wherein two
10 or more different probes are tethered to different locations of a support in the form of an array.
8. An array of oligonucleotides, for analysing a polynucleotide target containing a variable sequence, in which each component oligonucleotide i) comprises a sequence complementary to the target
15 including an expected variant of the target, and ii) is tethered to a solid support in a chemical orientation which a) permits duplex formation with the target, and b) permits chain extension only when the sequence of the oligonucleotide matches the variable sequence of the target.
9. A set or array of oligonucleotides, for analysing a
20 polynucleotide target containing a variable number tandem repeat sequence, in which each component oligonucleotide i) comprises a sequence complementary a part of the target immediately adjacent the repeat sequence, ii) comprises a sequence complementary to the repeat sequence of the target and containing a number of repeats expected in the
25 target, and iii) is configured in a way that a) permits duplex formation with the target, and b) permits chain extension only when the number of repeats in the oligonucleotide equals or is less than the number of repeats in the target.

10. A set or array as claimed in claim 9, wherein each component oligonucleotide iii) is configured in a way that b) permits chain extension: by ligation only when the number of repeats in the oligonucleotide equals the number of repeats in the target; or by polymerisation only when the number of repeats in the oligonucleotides is less than the number of repeats in the target.

11. A set or array of oligonucleotides as claimed in claim 9 or claim 10, wherein each component oligonucleotide is tethered to a solid support.

12. An array of oligonucleotides in which different oligonucleotides occupy different locations and each oligonucleotide has a 3' nucleotide residue through which it is covalently tethered to a support and a 5' nucleotide residue which is phosphorylated.

13. A method of making an array of different oligonucleotides tethered to different locations of a support, which method comprises the steps of: providing a first intermediate oligonucleotide tethered to the support and a second intermediate oligonucleotide in solution, and a third oligonucleotide that is complementary to both the first and second intermediate oligonucleotides, forming a duplex of the third oligonucleotide with the first and second intermediate oligonucleotides, and ligating the first intermediate oligonucleotide with the second intermediate oligonucleotide; and repeating the steps with oligonucleotides tethered to different locations of the support.